

§Appl. No. 10/088,356  
Amdt. dated February 17, 2004  
Reply to Office Action of, October 14, 2003

### **REMARKS**

#### **Drawings**

The objection to Fig. 11(B) has been noted. Applicant is now determining whether the sequences in the figure need to be added to the sequence listing.

#### **Rejection under §112, second paragraph**

Claims 6 and 47 have been amended. The amendment to claim 6 merely incorporates the features recited in claim 1, the claim upon which it was originally dependent. Therefore, its scope has not been altered in any way. Claim 47 was amended by the deletion of the phrase “in need of such treatment” since treatment is not necessary in the context of the claim.

#### **Rejection under §112, first paragraph**

Claim 6-10, 19, 21, 22, 25, 43-44, 47, and 84-89 are rejected under 112, first paragraph, allegedly as failing to comply with the written description requirement.

The specification provides numerous examples of genes selected in accordance with the claimed methods. For instance, Example 9 (Page 39) characterizes thirteen *M. tuberculosis* virulence genes identified by the inventors. See, also Figs. 8-15. The attached publication (Exhibit 1: Trucksis, M., ASM News, 66:668-674) provides several reasons (e.g., page 668) why the *M. marinum* model described in the present application would be recognized by a skilled worker as useful in identifying virulence genes in *M. tuberculosis*. For example: (1) both species are highly related both taxonomically and on a molecular level (e.g., on the basis of DNA-DNA hybridization studies) (e.g., Exhibit 1, Page 672, first column); (2) both species utilize highly similar pathogenic pathways (e.g., they multiply within phagocytic cells in a phagosome) (e.g., Exhibit 1, Page 672, Column 2), and (3) *M. marinum* mimics the pathophysiology of human tuberculosis.

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Moreover, genes identified using the *M. marinum* model have been shown to be virulence genes in *M. tuberculosis*, validating its use as a surrogate model. For example, at least three different classes of genes (Pks, PPE, and a transcriptional regulator with an AraC signature) were identified in the *M. marinum* screen, and were independently isolated in a mouse model using *M. tuberculosis*. See, Exhibit 2, Ruley et al., *FEMS Microbiology Letters*, 1-7 (in press, 2004), Section 3.5, 3<sup>rd</sup> paragraph. Thus, the inventors clearly had possession of the claimed methods and bacteria (e.g., claims 6-10, 19-22, 25, and 84-89).

“In order to make a rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (Examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the court, “it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.” 439 F.2d at 224, 169 USPQ at 370.” See, M.P.E.P. §2164.04.

There is also no reason to doubt that the avirulent bacteria of the present invention can be used to elicit an immune response (e.g., “to be antigenic,” Page 20, line 15; claim 47) or to utilize

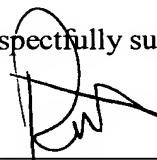
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as a vaccine. The bacteria of the present invention (as are any organism) are comprised of many different proteins which are antigenic and which would therefore be capable of at least producing an immune response in a host organism. There is simply no reasonable basis to question this fact.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

  
A handwritten signature in black ink, appearing to read 'R. Lebovitz', is written over a horizontal line.

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